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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/599,662	06/22/2000	Anita K. Hopper	PSU-04423	7492

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EXAMINER	
LAMBERTSON, DAVID A	

ART UNIT	PAPER NUMBER
1636	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/599,662	HOPPER ET AL.	
	Examiner	Art Unit	
	David A Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 September 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt is acknowledged of a reply, filed September 16, 2002 as Paper Nos. 10-13, to the previous Office Action. Acknowledgement is also made of a Petition to Revive the application after abandonment, as well as the granting of said Petition. Amendments were made to the claims. Specifically, new claims 17-21 were added.

Claims 1-21 are pending and under consideration in the instant application. Any rejection of record in the previous Office Action, Paper No. 7, mailed December 3, 2001, that is not addressed in this action has been withdrawn.

Election/Restrictions

Claims 17-19 have been joined with originally presented claims 1-16. Newly submitted claims 20 and 21 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the originally presented claims are drawn to a method of identifying a test compound that can act as an agonist or antagonist to the melvalonate pathway of sterol synthesis, whereas claims 20 and 21 are drawn to a method of screening for overexpressed genes. These inventions are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation, have different effects, and are not disclosed as being capable of being used together. Specifically, there is no step for necessarily providing cells with an overexpressed gene in the originally presented claims 1-16

and new claims 17-19, and there is no step for contacting cells with a test compound in claims 20 or 21, therefore the inventions require different, unrelated method steps hence the inventions have different modes of operation. Furthermore, the methods result in different outcomes, the identification of a test compound that serves as an agonist/antagonist (originally presented claims 1-16 and new claims 17-19) versus the overexpression of a gene (claims 20 and 21), therefore the methods have different effects. For example, the original claims would yield compounds that are not genes, whereas the newly added claims (20 and 21) would result in the identification of genes. Because the inventions have different modes of operation, different effects and are not disclosed as capable of being used together, the inventions are patentably distinct.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification (specifically, the original claims 1-16 and new claims 17-19 are classified in 435/29 and the newly added claims 20 and 21 are classified in 435/6), restriction for examination purposes as indicated is proper. In addition, a non-patent literature search of all of the claims would not be co-extensive due to the inventions having both different modes of operation and different effects, therefore said search would be burdensome.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 20 and 21 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Oath/Declaration

Applicant has supplied a new declaration in response to the previous Office Action. This declaration is acknowledged and overcomes the deficiencies cited in the previous Office Action.

Drawings

New corrected drawings are required in this application because of the reasons set forth in the Draftsperson's review form PTO-948, a copy of which is attached to this Office Action. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection not necessitated by amendment to the claims.**

Applicant claims a method of screening for compounds that are antagonistic or agonistic to the melvalonate pathway of sterol synthesis using modified yeast cells that express reduced cytosolic levels of Mod5p or its homolog. The claims read on a broad genus of proteins that can be used as homologs for Mod5p.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not sufficiently describe a representative number of species of the invention by actual reduction to practice or by disclosure of relevant identifying characteristics.

Applicant claims homologs of Mod5p by function only, without any disclosed or known correlation between the elements and their function. The specification only provides teachings regarding a Mod5p isozyme, and does not teach the use of homologs of Mod5p. Furthermore, the specification does not identify what structural or functional characteristics are required in order to determine if a protein is a homolog of Mod5p, nor does it identify the relevant structural features of Mod5p that are required for its use in the screen. As a result, the skilled artisan cannot envision a sufficient number of Mod5p homologs from the instant specification.

The prior art does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. There is no prior art disclosure of structural or functional features of the Mod5 protein that would allow the skilled artisan to envision what

constitutes a Mod5p homolog. Thus the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application or the prior art teaches a structure-function relationship for Mod5p in order to allow the determination of functional homologs of Mod5p. Without an adequate description of conserved amino acid residues or relevant domains of Mod5p that are required for its function, the skilled artisan would not be able to envision the claimed invention by relying on the teachings of the prior art or the instant specification. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection necessitated by amendment.**

Claims 1, 4, 7, 10, 12, 14 and 17 (and all dependent claims) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite because the claims do not recite a step that recapitulates the method as set forth in the preamble of the claim. Specifically, there is no positive process step that necessarily results in the identification of a test compound that is agonistic or antagonistic specifically to the melvalonate pathway of sterol synthesis, as stated in the preamble of the claim. The assay attempts to detect an agonist/antagonist *indirectly* by

measuring the activity of Mod5p, a protein that competes for a substrate that is an intermediate in the melvalonate pathway. However, because Mod5p is affected by numerous factors in different pathways besides the melvalonate pathway and because there is no step confirming that an identified compound has a specific effect on the melvalonate pathway, therefore the claim is indefinite.

Claims 11, 13 and 15 (and all dependent claims) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite because the claims refer to a method comprising measuring the growth and color of modified yeast cells harboring a nonsense mutation in either the *LYS2* or *CAN1* genes. These claims are indefinite because it is unclear what steps are taken to measure the color of these cells in the absence of a known color-producing phenotype for these mutants. Removing the limitation "and color" from these claims would be remedial.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Applicant is reminded that the preambles of the instant claims carry very little patentable weight in that there is no positive process step specifically identifying the compound as a specific agonist/antagonist of the melvalonate pathway. **This is a new rejection not necessitated by amendment.**

Claims 1-9 and 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Boguta *et al.* (*Gene* **185**:291-296, 1997, see entire document; henceforth Boguta).

Boguta teaches a screening method utilizing a modified yeast cell carrying the *maf1-1* mutation, the *mod5-1* mutation which results in reduced cytosolic levels of the Mod5p protein, the *ade2-1* nonsense mutation (see for example page 292-294, section 2.2) and which contains wild type levels of the tRNA suppression codon genes *SUP11* and *SUP7* (see for example Table 1). These cells are mixed with a test compound (specifically the plasmid p211/7 encoding Maf1), and then plated on growth media that was formulated to allow the scoring of nonsense suppression of the *ade2-1* gene (e.g., medium lacking adenine; see for example page 292-294, section 2.2). The cells are then monitored for their ability to suppress the *ade2-1* mutation by the ability to grow on medium lacking adenine without the accumulation of red pigment. (see for example page 293). Therefore, Boguta teaches each of the elements set forth in instant claims 1-9 and 17-19. Furthermore, and absent evidence to the contrary, Maf1 could be considered either an agonist or antagonist (depending on its expression/mutation state) to the melvalonate pathway by virtue of affecting the activity of Mod5p and in light of the asserted invention.

Claims 1-3 and 14-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Zoladek et al. (IDS reference 59; henceforth Zoladek). **This is a new rejection not necessitated by amendment.**

Zoladek teaches the use of a modified yeast cell, specifically comprising the *mod5-1* mutation which results in reduced levels of cytoplasmic Mod5p, the *lys2-1* nonsense mutation and wild type levels of the tRNA suppression codon genes *SUP11* and *SUP7*, in a screening

assay (see for example Table 1 on page 6885 and page 6887, the section concerning "Selection for mutants with altered mitochondrial-cytoplasmic distribution of Md5p-1, KR6). These cells were contacted with test compounds (UV-light or EMS; additionally, these compound modify nucleic acids in the cell, which can also be considered test compounds), and the cells were screened by virtue of their ability to grow on medium specifically formulated to screen for the suppression of the *lys2-1* nonsense mutation (by virtue of it lacking lysine), thereby monitoring the modulation of Mod5p activity (see for example page 6887). Therefore, Zoladek teaches all of the elements of instant claims 1-3 and 14-19. Furthermore, this screen resulted in the identification of the *mdp* genes, which resulted in increased Mod5p cytosolic activity upon their mutation (see for example page 6888, second full paragraph), therefore these genes could act either as agonists or antagonists to the melvalonate pathway by virtue of their effects on Mod5p, and depending on their expression/mutation state.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boguta as applied towards the rejections under 35 U.S.C. 102(b), and in view of Gillman et al. (IDS reference 21; henceforth Gillman). **This is a new rejection not necessitated by amendment.**

Briefly, Boguta teaches methods of screening a test compound for the ability to affect Mod5p activity by increasing the ability of Mod5p to activate suppressor tRNA codons via isopentenylation. Specifically, Boguta measures this activity by selecting for the ability of a strain to grow on specific growth medium that requires the suppression of a nonsense mutation, more specifically the *ade2-1* mutant.

Boguta does not teach using the *can1-100* nonsense mutation in their screens.

Gillman teaches that the activity of Mod5p, as it relates to the suppression of nonsense mutations, can be measured by monitoring the sensitivity of cells to the amino acid analog canavanine by using strains carrying the *can1-100* nonsense mutation (see for example page 2386-2387, the section on "Translation initiation site influences mitochondrial and cytoplasmic tRNA modification", and Table 3). Furthermore, Gillman also makes use of the *mod5-1* allele in order to diminish the cytoplasmic levels of Mod5p.

It would have been obvious to the ordinary skilled artisan to combine the teachings of Boguta with those of Gillman to result in the claimed invention because each reference uses the same activity (suppression of nonsense mutations) to monitor the activity of the same allele of the same protein (Mod5p), therefore the ordinary skilled artisan would have the expected benefit

of measuring the activity of Mod5p using three independent screening methods. In particular, the *can1-100* mutation has the added expected benefit of being a counter-selectable mutation. The ordinary skilled artisan would have been motivated to combine the teachings in order to obtain multiple means by which to test the activity of Mod5p, thereby decreasing the chances of a non-specific nonsense suppression or mutation affecting the outcome of the screen. Absent evidence to the contrary and given the teachings of the stated prior art and the high level of skill of the ordinary skilled artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zoladek as applied towards the rejection under 35 U.S.C. 102(b), and in view of Gillman et al. (IDS reference 21; henceforth Gillman). **This is a new rejection not necessitated by amendment.**

Briefly, Zoladek both teaches methods of screening a test compound for the ability to affect Mod5p activity by increasing the ability of Mod5p to activate suppressor tRNA codons via isopentenylation. Specifically, Zoladek measures this activity by selecting for the ability of a strain to grow on specific growth medium that requires the suppression of a nonsense mutation, more specifically the *lys2-1* mutant.

Zoladek does not teach using the *can1-100* nonsense mutation in their screens.

Gillman teaches that the activity of Mod5p, as it relates to the suppression of nonsense mutations, can be measured by monitoring the sensitivity of cells to the amino acid analog canavanine by using strains carrying the *can1-100* nonsense mutation (see for example page

2386-2387, the section on "Translation initiation site influences mitochondrial and cytoplasmic tRNA modification", and Table 3). Furthermore, Gillman also makes use of the *mod5-1* allele in order to diminish the cytoplasmic levels of Mod5p.

It would have been obvious to the ordinary skilled artisan to combine the teachings of Zoladek with those of Gillman to result in the claimed invention because each reference uses the same activity (suppression of nonsense mutations) to monitor the activity of the same allele of the same protein (Mod5p), therefore the ordinary skilled artisan would have the expected benefit of measuring the activity of Mod5p using three independent screening methods. In particular, the *can1-100* mutation has the added expected benefit of being a counter-selectable mutation. The ordinary skilled artisan would have been motivated to combine the teachings in order to obtain multiple means by which to test the activity of Mod5p, thereby decreasing the chances of a non-specific nonsense suppression or mutation affecting the outcome of the screen. Absent evidence to the contrary and given the teachings of the stated prior art and the high level of skill of the ordinary skilled artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
March 6, 2003

PATENT EXAMINER
Gerald G. Letters, Jr
A.U. 1636